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THE EFFECT OF IRREGULAR ABSORPTION ON GALAXY DISTRIBUTION

By Constance Warwick

Harvard College Observatory, Cambridge, Massachusetts

Communicated by Harlow Shapley, June 10, 1950

Introduction and Method of Analysis.—Recent researches[1-4] on interstellar absorbing material have emphasized the irregularity of its distribution. Greenstein[5] has found that the obvious large clouds near the Milky Way have diameters of the order of 100 pc., and photographic absorptions of about 1 mag., but that they account for only about one-ninth of the observed absorption. Spitzer,[6] summarizing recent investigations of smaller dark clouds assumed to be responsible for the remaining absorption, quotes the following values: average diameter, 16 pc.; mean photographic absorption per cloud, $0^m.23$; space density, between 1.0×10^{-6} and 1.2×10^{-4} clds./pc.^{3}.

The apparent distribution of galaxies offers an opportunity to study these small dark clouds. The methods outlined by Sterne[7] have been used to analyze the galaxy counts of Hubble.[8] The observations consist of galaxy counts made on plates taken at the Mount Wilson Observatory, and reduced to uniform ideal observing conditions. The fields are spaced at intervals of 5° in galactic latitude and approximately 10° in longitude, and each has an area of 0.6 square degree.

If there are discrete absorbing clouds, each with angular diameter large enough to cover two or more of the fields in which galaxy counts have been made, there will be a relation between the numbers of galaxies in adjacent fields. At each galactic latitude, we find for each field the residual from the mean number of galaxies per field for that latitude. The association test indicates whether the pattern of positive and negative residuals differs significantly from the pattern which would result if there were no irregular absorption. The correlation test is similar, but considers the size of the residuals, as well as the pattern.

The results of the tests are expressed by the value of P, the probability

that a value of the association (correlation) coefficient, equally or less probable than the value observed, should result from a random distribution. Thus $P = 1.00$ means that the observed distribution cannot be distinguished from a random distribution, while a very small value of P indicates that the observed distribution could hardly occur in the absence of some external effect on the numbers being analyzed. A value of P greater than 0.10, indicating that there is one chance in ten, or better, of finding the observed association in a random distribution, is not considered significant. The line between random and significantly non-random distributions is conventionally drawn at $P = 0.05$, while a value of P less than 0.02 may be considered to suggest strongly a departure from the laws of chance.

In applying the tests to the Mount Wilson galaxy counts, the fields at each galactic latitude were treated separately. The mean number of galaxies per field, $\bar{N}$, was found for the latitude zone, and the residual $x = (N - \bar{N})$ found for each field. The mean value, y, of the residual for the two adjacent fields was found, and the association and correlation coefficients between the values of x and y computed.

Let $N(x+)$ indicate the number of fields with positive residual x, $N(x+, y+)$ the number with positive x *and* positive y, etc. The association is clearly seen by making a table. The appropriate association coefficient

y \ x	+	−	
+	$N(x+, y+)$	$N(x-, y+)$	$N(y+)$
−	$N(x+, y-)$	$N(x-, y-)$	$N(y-)$
	$N(x+)$	$N(x-)$	n

has been given by Sterne.[7] In the present notation it is:

$$R = \frac{N(x+, y+) \cdot N(x-, y-) - N(x+, y-) \cdot N(x-, y+)}{\sqrt{\frac{N(x+) \cdot N(x-) \cdot N(y+) \cdot N(y-)}{(n-1)}}},$$

where n is the total number of fields in the latitude zone. Then $P(R)$ is given approximately by the area under the normal error curve corresponding to values of the abcissa numerically equal or greater than R. The correlation coefficient is given by

$$r = \frac{\sum xy}{\sqrt{\sum x^2 \cdot \sum y^2}}.$$

The value of $P(r)$ can be found from tables[9] if n is less than 30. If n is

equal or greater than 30, we take $P(r)$ equal to the area under the normal error curve corresponding to values of the abscissa numerically equal or greater than t where

$$t = \frac{r}{\sqrt{1 - r^2}} \cdot \sqrt{n - 2}.$$

The significance of the tests depends on the linear diameter of the smallest cloud that can be detected with this observational material. A rough estimate, assuming the space density of the clouds to be known, shows that the association test is not sensitive to the presence of clouds with linear diameter smaller than about 15 pc.

The Distribution at High Latitudes.—In order to separate intrinsic irregularities in the distribution of galaxies from irregularities caused by absorption, the data for galactic latitudes $\pm 40°$ to $\pm 60°$ were first examined. The frequency distribution of the numbers of galaxies per field was compared to the Poisson distribution, and found to have a much greater dispersion and definite asymmetry, with an excessive number of large positive residuals. (See Fig. 3, p. 7 of reference 10.) Association and correlation tests were applied to the high latitude distribution, and gave $P = 0.99$ and 0.62, respectively. From these results we conclude, first, that the large dispersion in the numbers of galaxies per field at high latitudes is caused largely by clustering, although perhaps partly by accidental magnitude errors and by the systematic correction of the actual counts; second, that the "clusters" are not large enough to affect more than a single field; and finally, that there are no dark nebulae present at these latitudes with large enough angular diameter to affect more than one field.

The Latitude Zones $+15°$ to $+30°$ and $-15°$ to $-30°$.—The number of fields with each value of $\log N$ was plotted against $\log N$ for each latitude zone (Fig. 1). In order to include in the frequency diagrams the fields in which no galaxies were found, the maximum possible value of $\log N$ was computed for each of the fields, assuming a uniform distribution of galaxies, and the density given by Hubble. For comparison with the observed curves, the theoretical distribution was computed assuming: (1) that the absorption is uniform (full drawn curves); and (2) that the absorption is caused by discrete clouds, each absorbing $0^m.23$, which are distributed over the sky according to Poisson's law (broken curves).

In the case of uniform absorption, the dispersion of the frequency distribution of the logarithms will increase as the number of galaxies per field decreases. The magnitude of this effect can be roughly estimated. If N_1 is the counted number in a given field, N the corrected number and a the correction factor, $N = aN_1$. For a random distribution, the dispersion in the counted number is equal to $\sqrt{N_1}$, and the dispersion in the cor-

rected number is $\bar{a}\sqrt{\bar{N}_1} \sim \sqrt{\bar{a}\bar{N}}$. The dispersion in the values of log N is approximately $0.43/\bar{N}$ times the dispersion in the values of N, or $0.43\sqrt{\bar{a}/\bar{N}}$. Since the frequency distribution of the logarithms of the numbers of galaxies per field for high latitudes is so closely represented by a normal distribution, we assume that the actual distribution of the logarithms is the result of two normal distributions, one, with dispersion s_0, caused by clustering and accidental errors, superimposed on the other with dispersion s_1 equal to the "natural uncertainty." s_0 is independent of galactic latitude, while s_1 increases with decreasing latitude. For the distribution resulting from the combination, the dispersion, s, will be given by

$$s^2 = s_0^2 + s_1^2 = s_0^2 + \frac{0.188\bar{a}}{\bar{N}}. \qquad (1)$$

The value of s_0^2 was found by substituting in (1) the values of s and $\bar{N}$ observed for the high latitude region. The value of s for each latitude was then found from (1). The normal error curve with dispersion s and mean log N for the latitude zone is the predicted frequency curve for uniform absorption.

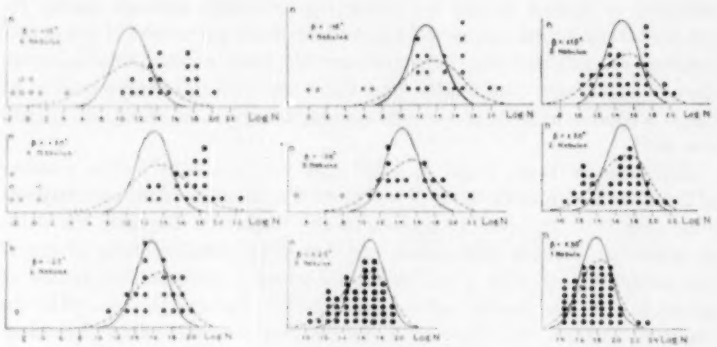

FIGURE 1

A Poisson distribution of the number of dark clouds along the line of sight was assumed in predicting the frequency of values of log N for the case that small dark clouds cause all the observed absorption. The mean value, $\Delta m(\beta)$, of absorption for each latitude zone was found from the relation

$$\log \bar{N}(\beta) = \log N_0 - 0.6\,\Delta m(\beta), \qquad (2)$$

where $\log N_0$ is the mean value of $\log N$ in the absence of absorption ($\log N$ for the high latitude region), and $\log N(\beta)$ is the mean value for the latitude zone under consideration. The mean number of dark clouds along the line of sight was taken as the nearest integer to $\Delta m/0^m.23$. The number of fields affected by 0, 1, 2, ... clouds was computed according to Poisson's law for each value of mean number of clouds along the line of sight. The frequency curve of $\log N$ for $\pm 40°$ to $\pm 60°$ was "smeared out" according to the Poisson distribution to give the predicted frequency curve.

A comparison of the predicted and observed frequency curves shows that neither hypothesis, small clouds or uniform absorption, explains the observed frequency when the fields in the zone of avoidance are included.

TABLE 1

All Fields

Association	$P > 0.10$	0.05–0.10	0.02–0.05	0.01–0.02	<0.01
	$-15°$		$+15°$		$\pm 20°$
	$-25°$		$+25°$		$\pm 30°$
Correlation	$-15°$	$+30°$			$+15°$
	$-25°$				$\pm 20°$
					$+25°$
					$-30°$
	Omitting Fields in Zone of Avoidance				
Association	$\pm 15°$		$+25°$		$\pm 20°$
	$-25°$				$\pm 30°$
Correlation	$-15°$	$+30°$	$+15°$		$+25°$
	$+20°$		$-20°$		$-30°$
	$-25°$				

As would be expected from Greenstein's work, we must assume larger clouds, or non-random accumulations of small clouds, to explain the zone of avoidance. When the fields in the zone of avoidance are omitted, the distribution of values of $\log N$ at positive and negative latitudes is sufficiently similar that we may combine $+15°$ with $-15°$, etc. The curves are shown in figure 1. We have not given the hypothesis of discrete clouds a completely fair chance to represent the observations, because the mean number of clouds was taken to be integral, so that the mean absorption for the predicted curve may not agree exactly with the observed mean. From these curves it appears that the discrete cloud hypothesis gives slightly better agreement with observation. More galaxy counts at low latitudes are needed to settle the question definitely.

The association and correlation tests were carried out as before, first including the fields in the zone of avoidance, and then omitting them. The results are given in table 1. We find that, even when the fields in the zone of avoidance are omitted, there is considerable evidence that the absorbing matter is not completely uniform. This may indicate the existence of clouds, or it may be caused by the fact that the absorption is stronger in the direction of the galactic center than in the opposite part of the sky. The data were corrected for this longitude effect, and the tests repeated. The correction was determined for each latitude (grouping $+15°$ with $-15°$, etc.) by plotting the residual $(N - \bar{N})$ against $\cos {}^1/_2(\lambda - \lambda_0)$, where λ is the galactic longitude of the field, and λ_0, the longitude of the galactic center, was taken as 325°. A straight line was drawn through the points, from which the mean residual at each longitude was found and subtracted from the residual for the field. The corrected residuals (with fields in the zone of avoidance omitted) show association with $P > 0.10$ for all latitude zones except that at $+25°$, which has $0.02 < P \leq 0.05$. The correlation test gives $P < 0.01$ for the zone at 30°, $0.02 < P \leq 0.05$ for those at $+15°$ and $+25°$, and $P > 0.10$ for all other zones. From these results we conclude that the small dark clouds, if they exist, are smaller than the critical diameter, 15 pc., to which the tests are sensitive.

The Dispersion at Low Latitudes.—The frequency distribution of log N shows that the observed dispersion is generally greater than that predicted for uniform absorption. The observed dispersions in the values of log N were tested to find the probability that as large or larger dispersion be found if the absorption is uniform. The dispersion for uniform absorption, s, was predicted by equation (1). If s' is the observed dispersion, and n the number of fields, $\chi^2 = s'^2/s^2$, and the desired probability, $P(\chi^2)$, can be found from tables[9] when $n \leq 30$. If $n > 30$, we compute $m = \sqrt{2\chi^2} - \sqrt{(2n - 3)}$, and use the approximation

$$P = \frac{2}{\sqrt{2\pi}} \int_{|m|}^{\infty} e^{-x^2/2}\, dx.$$

The dispersion depends on the number of dark nebulae along the line of sight, and so, since the total absorption is known, on the value of τ, the absorption of a single cloud. We estimate the minimum value of τ which will result in a significant dispersion. Suppose that, in a given latitude zone, values of the number of dark clouds along the line of sight, n, are distributed about the mean, $\bar{n}$, according to Poisson's law, with dispersion $\sqrt{\bar{n}}$. Substituting in (2), $\Delta m(\beta) = n(\beta)\tau$, we find

$$\log N(\beta) = \log N_0 - 0.6n(\beta)\tau.$$

The dark clouds cause a dispersion in log N equal to $0.6\,\tau\sqrt{\bar{n}(\beta)}$. We find for the observed dispersion, using (1);

$$s^2 = s_0^2 + \frac{0.188\bar{3}}{\bar{N}} + 0.36\ \overline{\Delta m(\beta)}\tau. \qquad (3)$$

Substituting values of the constants for $+15°$, we find that if $P \leq 0.10$, $\tau \geq 0^m.05$.

The dispersion test was made only on the residuals in log N corrected for the longitude effect. Fields for which the correction factor exceeded 3.5, and those noted by Hubble as in the zone of avoidance or containing a cluster were omitted. For the zone at $-15°$, $P < 0.01$, while $0.02 < P \leq 0.05$ at $+15°$, and $0.05 < P \leq 0.10$ at $-20°$; $P > 0.10$ for all other zones.

Recomputation of Value of τ.—In his analysis of the Mount Wilson galaxy counts, Ambarzumian[2] has made the tacit assumption that the dispersion in the number of galaxies per field is caused entirely by irregularities in absorption. A repetition of his analysis, taking into account the tendency of galaxies to cluster, gives a value of τ, the mean absorption of one dark cloud, considerably smaller than that found by Ambarzumian.

The values of log N given in Mount Wilson Contribution 485 for latitudes $\pm 15°$ to $\pm 85°$ were used in the analysis, omitting fields for which the correction factor exceeds 3.5, fields in or near the zone of avoidance, and fields containing conspicuous clusters. (See table XI, p. 41 of reference 8.) The mean value of s^2, the square of the observed dispersion in log N for a given zone, was plotted against csc $|\beta|$ for each $|\beta|$. Assuming the relation $s^2 = a + b \csc |\beta|$, a least squares solution was made for the constants a and b. The solution depends strongly on the values for $\pm 15°$ and $\pm 20°$; the values for higher latitudes show no relation to the latitude.

In (3) we substitute $\overline{\Delta m(\beta)} = 0.25 \csc |\beta|$ and $\log N(\beta) = \log N_0 - 0.6\,\Delta m(\beta)$. Using the approximation $N^{-1} = N_0^{-1} 10^{0.15 \csc |\beta|}$ and using the first two terms of the Taylor expansion, we get

$$s^2 = s_0^2 + \frac{0.188}{N_0} + \left[\frac{0.188}{N_0} \cdot \frac{0.15}{0.43} + 0.09\tau\right] \csc |\beta|.$$

Setting the coefficient of csc $|\beta|$ equal to 0.00823, the value of b found from the least squares solution, and substituting $N_0 = 82.4$, we find $\tau = 0^m.08$.

The smaller value of τ leads to different values of the other constants which describe the distribution of the absorbing matter, assuming that it occurs in the form of small clouds. Spitzer gives the relations

$$A = k\tau \qquad (4)$$

$$k = 1000\pi r^2 D, \qquad (5)$$

where A is the total photographic absorption in magnitudes per kiloparsec, k is the number of clouds per kiloparsec along a line of sight, D is the number of clouds per cubic parsec and r is the average radius of a cloud. If we assume that $0^m.1$ is an upper limit for the value of τ, then we find from (4) that 16 is a lower limit for k. If τ is as small as $0^m.1$, the effect of a single cloud on a galaxy field will not be distinguishable from random variations in the numbers of galaxies, and our conclusions from the association and correlation tests as to the size of the clouds are meaningless. However, let us assume that the average radius is 10 pc. Then we find that D, the number of clouds per cubic parsec, is at least as great as 5×10^{-5}, and that the average distance between clouds is only about 27 pc. Acceptance of these conclusions from the galaxy distribution leads us to a picture very close to uniformity.

Galaxy counts over large areas in low galactic latitudes would greatly increase the value of this sort of analysis. Such data should smooth out the observed frequency distribution curves, so that a trial and error fitting of a Poisson distribution would indicate the mean value of absorption of a single cloud. These counts would add to the sensitivity, as well as to the significance of the association and correlation tests. By grouping areas of one square degree into larger areas, and finding at which area the association enters, an estimate of the mean diameters would be possible.

Conclusions.—(1) The distribution of galaxies between galactic latitudes $\pm 40°$ and $\pm 60°$ shows that there are clusters of galaxies, but there is no evidence of irregular absorption at these latitudes.

(2) The frequency distributions of log N suggest that the absorbing material at $\pm 15°$ to $\pm 30°$ and outside the zone of avoidance may be condensed into small clouds, but more observations are needed to show definitely that the absorption is not uniform. The large dark nebulae of the Milky Way cannot be explained as random accumulations of small clouds.

(3) The positive association and correlation between residuals in neighboring fields are caused at least partly by the fact that the absorption is stronger toward the galactic center than toward the anti-center. If the absorbing material occurs mainly in clouds, they are not larger than about 15 pc. in diameter.

(4) The dispersion in values of log N does not differ significantly from that predicted for uniform absorption, indicating that the value of τ, the absorption of a single cloud, is not much greater than $0^m.05$. A recomputation of the value of τ, following the method of Ambarzumian, but considering the clustering of galaxies and the increase in dispersion due to uniform absorption, gives $\tau = 0^m.08$.

I would like to express appreciation for the assistance of Dr. Bart Bok, who suggested this investigation and has guided its progress.

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[10] Bok, B. J., *H. B.*, **895**, 1 (1934).

THE MECHANISM OF ACTION OF A BACTERIAL TOXIN ON PLANT CELLS

BY ARMIN C. BRAUN

THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH, NEW YORK, N. Y.

Communicated by L. O. Kunkel, June 23, 1950

An attempt has been made in this investigation to account in biochemical terms for a toxemia associated with the wildfire disease of tobacco. Wildfire, a bacterial disease, the causal agent of which is *Pseudomonas tabaci*, is characterized by localized chlorotic halos 1 to 2 cm. in diameter (Fig. 1*a*) that surround a central brown necrotic spot that is usually but not always quite small in size. The chlorotic area is free of bacteria and results from the diffusion of a toxic substance secreted by the bacteria present in the central necrotic focus of infection. In young tobacco plants the toxin may become systemic, diffusing throughout the plants and frequently killing them. Losses resulting from seedbed infection of the disease may thus be very high.

P. tabaci produces the toxin freely on a variety of culture media as well as in the host.[1-3] This substance can be separated from the bacteria by filtration and the sterile culture filtrates are capable of reproducing the toxic manifestations of the wildfire disease not only in tobacco but also in a large number of plant species representing many different families.[1] It has been suggested[2] that the toxin owes its biological activity to its chemical affinity for the chlorophyll molecule.

Materials and Methods.—In studying the mode of action of the wildfire toxin the unicellular plant *Chlorella vulgaris* was selected as the test object. Chlorella develops well on a simple readily reproducible medium of the following composition: KNO_3 1.5 g., $Ca(NO_3)_2 \cdot 4H_2O$ 1.5 g., $MgSO_4 \cdot 7H_2O$ 2.4 g., KH_2PO_4 2.4 g., $FeSO_4$ 0.02 g., $MnSO_4 \cdot 4H_2O$ 0.001 g., H_3BO_4

0.001 g., $CuSO_4$ 0.0001 g., $ZnSO_4 \cdot 7H_2O$ 0.0001 g., sucrose 20 g., distilled H_2O 1000 cc.

In these studies the cultures were grown in 50-cc. Erlenmeyer flasks. The basic medium together with supplementary substances totaling 10 cc. were placed in each flask. Sterilization was accomplished in an autoclave at 10 pounds' pressure for 10 minutes. Heat-labile compounds as well as the wildfire toxin were sterilized by filtration through Jena sintered glass

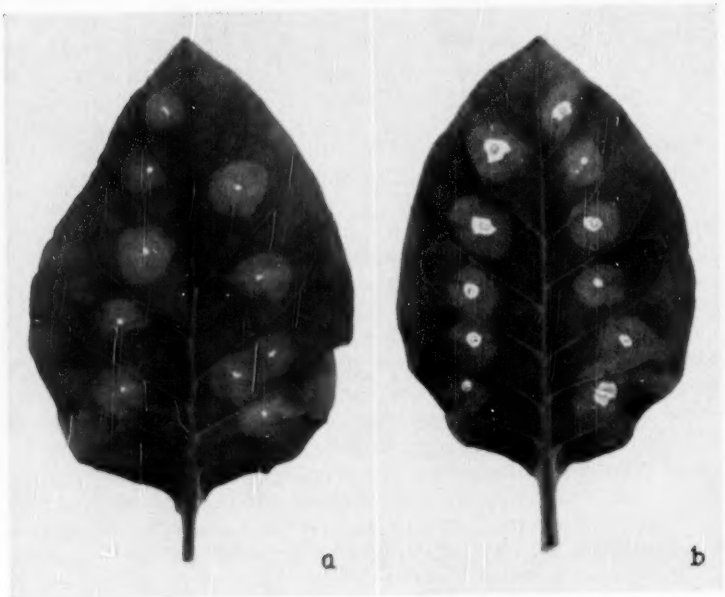

FIGURE 1

Tobacco leaves inoculated with (*a*) sterile wildfire toxin, (*b*) methionine sulfoximine. Note the similarity of chlorotic halos produced around the points of inoculation by the two substances.

bacteriological filters, porosity G 5 on 3. These compounds were added aseptically to the basic medium at the desired concentration. The flasks were inoculated with one drop of a one-week-old culture of Chlorella. Cultures were permitted to develop in an incubator at 26°C. for 5 days unless otherwise stated.

The partially purified toxin used in these experiments was prepared in the following manner. The bacteria were grown in large flasks containing a

solution of mineral salts and sucrose for 4 days at 25°C. The medium was well aerated during the incubation period. Following incubation the organisms were removed from the solution by centrifugation and the filtrate was treated with norite A at a pH of about 6.5. The adsorbed toxin was eluted with methanol and the methanol was removed by distillation under vacuum at a temperature not exceeding 35°C. The resulting residue was taken up in the medium used for growing Chlorella. The solution was standardized by adding enough basic media so that when assayed on tobacco leaves the toxin-containing solution produced a halo 5 mm. in diameter at a dilution of 1–100. Sterilization of this preparation was accomplished by filtration through a sintered glass filter. The stock toxin solution which was stored at 4°C. was used for all experiments reported here.

Experimental Results.—When growth of Chlorella in a medium containing dilute wildfire toxin (the medium gave a faint halo at a dilution of 1–5 when tested on tobacco) was compared with growth in a similar but non-toxin-containing medium, it was found that multiplication of the organism, although not completely inhibited, was only about one-third as rapid in the former as it was in the control medium after a 12-day incubation period. High concentrations of toxin completely inhibited growth of Chlorella. These results suggested that the toxin either interfered with synthesis of some essential growth factor or impaired the ability of Chlorella to utilize such a factor. In testing these possibilities it was found that when a medium containing toxin in a concentration sufficient to inhibit completely the growth of Chlorella (the medium gave a halo 5 mm. in diameter at a dilution of 1–50 when tested on tobacco leaves) was supplemented with 0.5 per cent liver extract, the deleterious effect of the toxin on the growth of the organism was completely negated. The toxin itself was not inactivated by the liver extract. The liver extract, therefore, contained a factor or factors necessary for the growth of Chlorella that were rendered unavailable for normal growth of that organism as a result of the action of the toxin.

A large number of compounds, among which were included the water-soluble vitamins, the amino acids, representative purine and pyrimidine derivatives, certain sulfhydryl compounds, as well as other substances known to be present in liver extract, were tested individually in an attempt to find the factor present in the liver extract capable of overcoming the toxic influence. Of these only one, *dl*-methionine, was capable of completely neutralizing the deleterious effect of the toxin on the growth of Chlorella. Growth of Chlorella in a toxin-containing medium supplemented with 0.1 mg./cc. of *dl*-methionine was comparable in every respect to the growth of the organism on a non-toxin-containing control medium. The natural form of methionine was found to be active, while the *d* isomer was entirely without effect. Certain other amino acids, such as *dl*-leucine, *dl*-norleucine and to a lesser extent *l*+arginine, *dl*-phenylalanine and *l*-tyrosine, were partially

effective in neutralizing the toxic influence when relatively small concentrations of toxin were present in the culture medium.

The probable pathway of methionine synthesis has been established for a number of different organisms. The following scheme with minor variations, cysteine → cystathionine → homocysteine → methionine, appears to hold for *Bacillus subtilis*,[4] *Escherichia coli*[5, 6] and Neurospora.[7] When tested separately, however, *l*-cystathionine and *dl*-homocysteine were found to be ineffective in overcoming the toxic influence on the growth of Chlorella. *l* + cysteine was found to be quite toxic for the organism.

If the synthesis of methionine in Chlorella follows a pathway similar to that reported for certain other organisms, then it would appear that either (1) a metabolic block occurs in the final step in the synthesis of methionine, possibly by virtue of the fact that the toxin prevents the methylation of homocysteine, or (2) that *l*-methionine is being synthesized by the organism in the presence of the toxin but that the toxin prevents the normal utilization of that compound. In order to determine which of the two possibilities was involved here, the growth of Chlorella in three different concentrations of toxin was tested against a range of concentrations of *l*-methionine. In this experiment the toxin-containing media, when assayed on tobacco leaves, produced halos 5 mm. in diameter at a dilution of 1–50, 1–25 and 1–10, respectively. When the data obtained following a 3-day incubation period were plotted it was found that the resulting curves were characterized over a range of concentrations by a more or less constant ratio between metabolite and inhibitor. Partially purified toxin was used in these experiments, however, and the final interpretation of results obtained in this phase of the work is withheld until the experiments can be repeated with chemically pure toxin. The results obtained with the impure preparation nevertheless suggest that the toxin-methionine antagonism is competitive, indicating that *l*-methionine is being synthesized by Chlorella in the presence of the toxin but that normal utilization of that compound is impaired by the action of the toxin.

While it has been possible to reverse completely the deleterious effect of the toxin on the growth of Chlorella with *l*-methionine, a similar reversal has not yet been possible when tobacco leaves containing chlorotic halos were immersed in a solution of that compound. That the mechanism of action is similar in both organisms, however, is suggested by the fact that the known methionine antagonist, methionine sulfoximine, in a concentration of 0.1 mg./cc. produced chlorotic halos in tobacco leaves that were indistinguishable from those produced by the wildfire toxin, as shown in Figure 1*b*.

Summary and Conclusions.—The bacterial toxin associated with the wildfire disease of tobacco has been shown to exert its biological effect by interrupting the methionine metabolism of plant cells.

The inhibitory influence of the toxin on the growth of Chlorella was completely reversible in the presence of *l*-methionine. A similar reversal has not yet been accomplished in tobacco. That the mechanism of action is similar in both organisms, however, is suggested by the fact that methionine sulfoximine, a known methionine antagonist, produced chlorotic lesions in tobacco leaves that were indistinguishable from those produced by the bacterial toxin.

The author is greatly indebted to Professor Vincent du Vigneaud, Department of Biochemistry, Cornell University Medical School, for the *l*-cystathionine and *dl*-homocysteine, and to Dr. L. Reiner, Wallace and Tiernan Products, Inc., for the methionine sulfoximine used in these studies.

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*THE GROWTH-PROMOTING PROPERTIES OF QUINIC ACID**

BY MALCOLM GORDON,† FRANCIS A. HASKINS‡ AND HERSCHEL K. MITCHELL

THE KERCKHOFF LABORATORIES OF BIOLOGY,
CALIFORNIA INSTITUTE OF TECHNOLOGY, PASADENA

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Evidence is accumulating that there is a common metabolic precursor to many of the benzene ring derivatives found in living organisms[1–4]. Recent work by Davis[3] and Tatum[4] indicates that one such precursor is the naturally occurring shikimic acid (Fig. 1) since this compound serves as a growth factor for certain mutants of *Escherichia coli*[3] and Neurospora[4] which otherwise require a combination of tyrosine, phenylalanine, tryptophan and *p*-aminobenzoic acid for growth. These mutants cannot utilize the closely related, naturally occurring quinic acid (Fig. 1) as a substitute for any of their requirements.[3, 4]

In an earlier investigation of quinic acid and shikimic acid, Fischer and Dangschat[5, 6] showed that quinic acid is chemically convertible to shikimic

acid and that the latter is convertible to glucodesonic acid. They pointed to the possibility that these compounds are formed directly from glucose.

For these reasons the growth-promoting properties of quinic acid and shikimic acid were reinvestigated with a Neurospora mutant, C-86, which is capable of utilizing a variety of aromatic compounds for growth[2, 7, 8]. Table 1 gives a list of compounds utilized by C-86 together with those utilized by several other mutants used in this investigation[2, 7–9].

Experimental.—Methods: The growth responses of the several strains of Neurospora tested were measured as dry weight of mycelium after 120 hours at 25° in 20 ml. of the standard Fries medium, adjusted to pH 4.6. Inoculations were made with drops of suspensions of conidia in sterile water. The shikimic acid[10] and the quinic acid[11] were filter sterilized and added sterilely to the autoclaved medium after cooling.

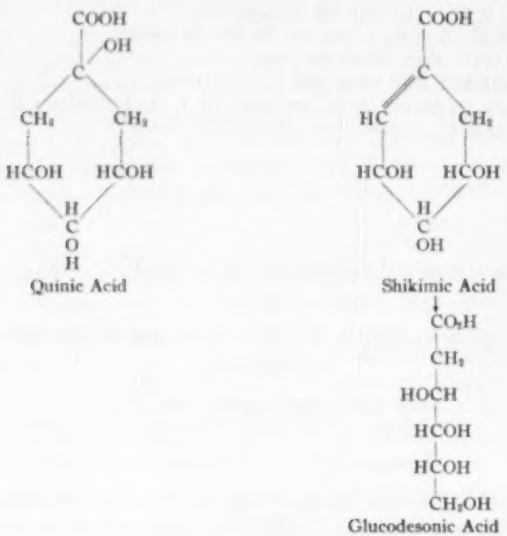

FIGURE 1

Analytical: The quinic acid used was recrystallized from water, melted at 162–163° and had a molecular rotation of −42.8° at 25°. Calculated, C, 43.75, H, 6.29; found, C, 43.49, H, 6.18.

Responses of Mutant Strains: The following compounds were tested for their ability to promote the growth of Neurospora, strain C-86: shikimic acid, quinic acid, dopa, protocatechuic acid, *p*-aminobenzoic acid and gentisic acid. Except for a very small response to gentisic acid, quinic acid

is the only one of these which supports the growth of C-86. Table 2 compares this effect with the growth-promoting effect of tryptophan.

While the activity of quinic acid is about the same as that reported for tyrosine and *trans*-cinnamic acid at low levels,[2] the inhibitory effect noted at higher concentration with *trans*-cinnamic acid is not observed with quinic acid.[12]

To eliminate the possibility that the growth response of C-86 to quinic acid is due to contamination with small amounts of other compounds which promote its growth (table 1), the same sample of quinic acid was filter sterilized and tested at 1- and 5-mg. levels against each of the other mutants listed in table 1. None grew at either concentration of quinic acid.

TABLE 1

COMPOUNDS UTILIZED BY VARIOUS NEUROSPORA MUTANTS

STRAIN	TYROSINE OR *trans*-CINNAMIC ACID	PHENYL-ALANINE	ANTHRA-NILIC ACID	INDOLE	TRYPTO-PHAN	KYNURE-NINE	3-OH-KYNURE-NINE	3-OH-ANTHRA-NILIC ACID	NICO-TINIC ACID
C-86	+	+	+	+	+	+	+	+	+
E-5212	−	+	−	−	−	−	−	−	−
B-1312	−	−	+	+	+	+	−	−	−
39401	−	−	−	+	+	+	+	+	+
10575	−	−	−	+	+	−	−	−	−
C-83	−	−	−	−	+	−	−	−	−
E-5029	−	−	−	−	−	−	+	+	+
4540	−	−	−	−	−	−	−	−	+

TABLE 2

GROWTH OF NEUROSPORA MUTANT C-86 IN THE PRESENCE OF (−)-QUINIC ACID AND *L*-TRYPTOPHAN

γ	DRY WT. OF MOLD, MG.	
	L-TRYPTOPHAN	(−)-QUINIC ACID
25	15.8	...
50	22.8	...
100	33.6	...
250	...	2.0
500	69.2	7.6
1000	...	21.8
3000	...	38.4
5000	...	48.2

Discussion.—These experiments demonstrate three main differences between the shikimic acid and quinic acid mutants of Neurospora.

(1) The mutant which utilizes shikimic acid cannot utilize quinic acid and vice versa.

(2) C-86 grows in the presence of any one of a number of compounds which presumably are related metabolically. The shikimic acid mutant requires four aromatic compounds for growth in the absence of shikimic acid.

(3) *p*-Aminobenzoic acid has no effect on C-86, while it is an absolute requirement for the shikimic acid mutant in the absence of shikimic acid.

The apparent lack of correlation between the results obtained with C-86 and the shikimic acid mutant can be explained by one of several schemes. However, the data presently available do not warrant extensive speculation about the presumed metabolic relationship between quinic acid and shikimic acid, between them and glucose or between them and the aromatic compounds they replace. The evidence would nevertheless seem to favor the view that at least several of the aromatic compounds found in Neurospora arise from a common non-aromatic, cyclical intermediate.

Summary.—Quinic acid promotes the growth of Neurospora, strain C-86, which otherwise requires for growth any one of several aromatic compounds. The closely related shikimic acid is completely without activity for this strain.

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† Merck Fellow of the National Research Council.

‡ Atomic Energy Commission Predoctoral Fellow.

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FURTHER STUDIES ON THE PURINE AND PYRIMIDINE METABOLISM OF TETRAHYMENA*

BY G. W. KIDDER, VIRGINIA C. DEWEY, R. E. PARKS, JR., AND M. R. HEINRICH

BIOLOGICAL LABORATORY, AMHERST COLLEGE

Communicated by A. F. Blakeslee, June 14, 1950

Introduction.—It has been shown that the animal microorganism, Tetrahymena, possesses a pattern for the metabolism of purines and pyrimidines which is at variance with other animals so far critically studied. Unlike higher animals, Tetrahymena has lost capacities for the synthesis of certain purines and pyrimidines. Thus it was shown[1] that of the naturally occurring purines only guanine would satisfy its requirement. Adenine and hypoxanthine are metabolized, however, since both show guanine sparing action. Xanthine was found to be inactive. It was likewise shown that only uracil, of the naturally occurring pyrimidines, would satisfy the pyrimidine requirement of Tetrahymena. Unlike the purine specificity, however, a block occurs which makes it impossible for the organism to carry out the riboside linkage with cytosine, for either cytidine or cytidylic acid will replace uracil, uridine or uridylic acid.

By the use of a number of substituted purines[2] and pyrimidines,[3] it was possible to gain some information as to the specific metabolic abilities of this organism regarding these important classes of compounds. It was shown, for instance, that of the methyl-substituted xanthines all were inert or inhibitory with the single exception of 1-methyl xanthine. This latter compound would replace guanine with 15 per cent activity. Methyl substitutions on the guanine molecule reduced its activity for guanine replacement. 1-Methylguanine was 75 per cent as effective as guanine, and 7-methylguanine and 1,7-dimethylguanine were weakly active in sparing guanine. Any substitution on the uracil molecule reduced the activity to 1 per cent or less.

Inasmuch as the metabolic pathways for nucleic acid constitutents have assumed considerable importance, it is the purpose of this paper to report extensions of our previous findings and to compare briefly the biosynthetic abilities of Tetrahymena with those of other organisms.

Experimental.—*Tetrahymena geleii* W, grown in pure (bacteria-free) cultures, was used throughout this work. The basal medium used is given in table 1. A new technique using the Brewer Automatic Pipetting Machine, described elsewhere,[4] was used for accuracy and speed. Quantitative growth determinations were made turbidimetrically by use of a Lumetron photoelectric colorimeter with a red (650) filter. The tubes were incubated at 25°C. for 96 hours in a slanted position for adequate aeration.[5] All

series were run in triplicate and the experiments repeated varying numbers of times.

Results.—The imidazole ring: It was earlier reported[6] that Tetrahymena was able to synthesize guanine from 2,4-diamino-5-formylamino-6-hydroxy pyrimidine. The latter compound was said to possess 13.5 per cent activity when compared to guanine hydrochloride dihydrate on a weight basis.

TABLE 1

BASAL MEDIUM[a]

DL-alanine	110	$MgSO_4 \cdot 7H_2O$	100.00
L-arginine HCl	206	$Fe(NH_4)_2(SO_4)_2 \cdot 6H_2O$	25.00
L-aspartic acid	122	$FeCl_2 \cdot 6H_2O$	1.25
Glycine	10	$MnCl_2 \cdot 4H_2O$	0.50
L-Glutamic acid	233	$ZnCl_2$	0.05
L-histidine HCl	87	$CaCl_2 \cdot 2H_2O$	50.00
DL-isoleucine	276	$CuCl_2 \cdot 2H_2O$	5.00
L-leucine	344	K_2HPO_4	1000.00
L-lysine HCl	272	KH_2PO_4	1000.00
DL-methionine	248	Dextrose	2500.00
L-phenylalanine	160	Na acetate	1000.00
L-proline	250	Tween 85[b]	700.00
DL-serine	394	Guanylic acid[c]	30.00
DL-threonine	376	Adenylic acid[c]	20.00
L-tryptophane	72	Cytidylic acid[c]	25.00
DL-valine	162	Uracil[c]	10.00
Ca pantothenate	0.10	Protogen[d]	1 unit
Nicotinamide	0.10		
Pyridoxine HCl	1.00		
Pyridoxal HCl	0.10		
Pyridoxamine HCl	0.10		
Riboflavin	0.10		
Pteroylglutamic acid	0.01		
Thiamine HCl	1.00		
Biotin (free acid)	0.0005		
Choline Cl	1.00		

[a] All amounts are given in micrograms per ml. of final medium.

[b] Atlas Powder Company.

[c] Omitted in appropriate experiments.

[d] Furnished by the Lederle Research Laboratories through the courtesy of Dr. E. L. R. Stokstad.

Since that report, different samples of the formylamino compound have been used, and it has been found that the original sample contained approximately 9 per cent guanine (on a molar basis) as a contaminant. The presence of guanine was shown by the fact that the activity for Tetrahymena was not diminished by a hydrolysis which completely destroyed the formylamino compound. The absence of the formylamino compound in hydrolyzed samples was demonstrated by ultra-violet absorption measure-

ments. Other samples of the formylamino pyrimidine, free of guanine contamination, had no activity for Tetrahymena either before or after hydrolysis. It is apparent, therefore, that this organism does not possess the necessary enzymes for the dehydration of 2,4-diamino-5-formylamino-6-hydroxy pyrimidine and is incapable of forming the imidazole ring. As might be expected, 2,4-diamino-5-acetylamino-6-hydroxy pyrimidine and 2,4-diamino-5-propionylamino-6-hydroxy pyrimidine were inert, as was 2,4,5-triamino-6-hydroxy pyrimidine.

Tetrahymena is able to demethylate position 8 of guanine to some extent (8-methyl guanine was 5 per cent as active as guanine), but 8-ethyl guanine[7] is inert.

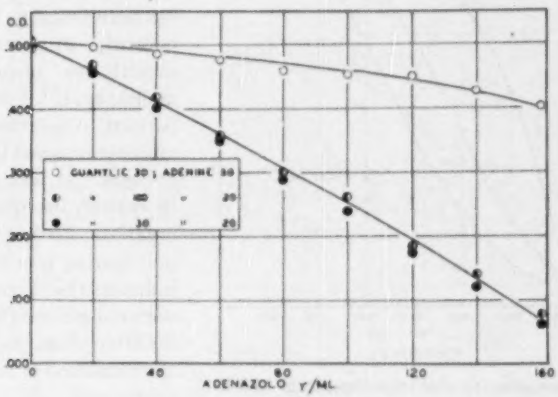

FIGURE 1

Release of the inhibition caused by 7-amino-1-v-triazolo(d)-pyrimidine (adenazolo) by adenine, but not by guanylic acid. The amounts of guanylic acid and adenine are in γ/ml. Guanine and hypoxanthine, like guanylic acid, do not release.

Triazolo analogs: It was previously reported[2] that the triazolo analog of hypoxanthine (7-hydroxy-1-v-triazolo(d)pyrimidine) was not inhibitory to Tetrahymena within the ranges tested. This finding, when considered in relation to the activity of the adenine analog (7-amino-1-v-triazolo(d)-pyrimidine) to be considered below, assumes importance in evaluating the metabolism of hypoxanthine and adenine by this organism.

The adenine analog, which we shall call adenazolo in keeping with the previous nomenclature of these compounds,[8] is an active purine inhibitor with an inhibition index (half maximum) of 5. This inhibition is specifically reversed by adenine. Guanine and hypoxanthine are inactive. A typical experiment is illustrated in Figure 1 showing the inability of guanine to re-

verse the adenazolo inhibition. It is to be remembered that both hypoxanthine and adenine are active in sparing guanine, and it was suggested[2] that hypoxanthine might be used by Tetrahymena for the synthesis of inosinic acid. It now appears more likely that the sparing action of hypoxanthine is due to its ready amination to adenine; when this system is blocked (by hypoxanthazolo), it is of little importance and no effect is noted.

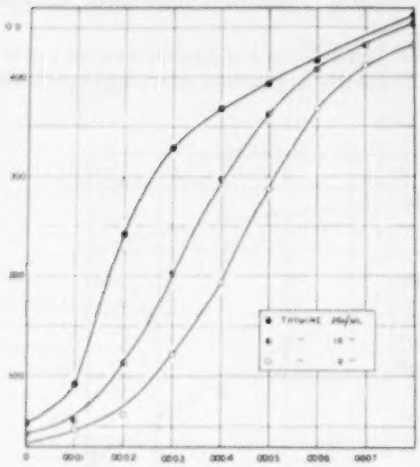

FIGURE 2

Dose response to pteroylglutamic acid (PGA) in media with and without thymine. The basal medium contained the following nucleic acid components in γ/ml.: guanylic acid, 30; adenylic acid, 20; cytidylic acid, 25; uracil, 10. Under the conditions of these experiments half maximum growth in the medium devoid of thymine required approximately 0.00046 γ/ml. of PGA; with 10 γ/ml. of thymine this requirement was reduced to 0.00035 γ/ml. and with 20 γ/ml. of thymine the requirement was further reduced to 0.00021 γ/ml. Raising the level of thymine up to 50 γ/ml. resulted in no greater sparing action than 20 γ/ml. of thymine.

Pyrimidines. Orotic acid: Inasmuch as orotic acid (4-carboxyuracil) has been found to have activity for certain pyrimidine-less Neurospora mutants[9, 10] and has been found to be incorporated, in contrast to uracil, in mammalian nucleic acid,[11, 12] it was important to test the activity of this compound for Tetrahymena. It was found to be entirely inactive for this organism, neither replacing nor sparing uracil.[13] This indicates that Tetrahymena does not possess the specific decarboxylase necessary for the formation of uracil from orotic acid. It cannot be shown, therefore, whether or not orotic nucleoside can be formed, as occurs in the mammal,[12] although this appears unlikely.

Thymine and thymidine: Our data indicate that thymine is not formed by the methylation of uracil but is synthesized by Tetrahymena from non-pyrimidine precursors. It was earlier reported[2] that neither thymine nor thymidine could replace uracil, and critical quantitative tests now show that neither has any sparing action. This would not be true if some uracil or uridine were being used for their synthesis. Moreover thymine is active in sparing pteroylglutamic acid (Fig. 2) which is taken to mean that PGA

is active in one or more steps in the synthesis of thymine. Thymidine[14] is approximately twice as active as thymine as a sparer of PGA, indicating that PGA may function also in performing the desoxyriboside linkage. These observations are in agreement with those on *Lactobacillus casei*[15, 16] and *Streptococcus fecalis*[16, 17] where thymine was found capable of replacing PGA. Tetrahymena differs from these bacteria, however, in that thymine and thymidine will only spare, never replace, PGA. One or more vital functions in the metabolism of this animal, in addition to those concerned with thymine and its desoxyriboside, are PGA controlled.

Discussion.—We can now reconstruct a probable course of metabolic pathways in Tetrahymena for purines and pyrimidines and compare these to what has been learned about these compounds in other organisms.

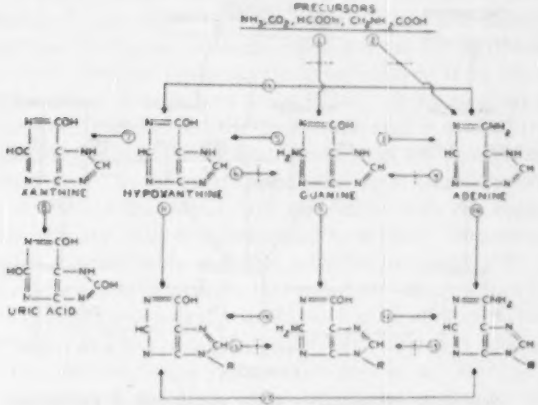

FIGURE 3

Schematic representation of the metabolism of purines. The dotted lines represent blocks in specific enzyme systems which occur in Tetrahymena. For evidence see text.

Figure 3 is a summary of the various steps in the metabolism of purines. The dotted cross lines on the arrows refer to blocks in the enzyme systems of Tetrahymena.

Reactions 1 and/or 2 are known to occur in the rat and pigeon, where it has been shown by tracer techniques that the purine ring is built up as follows: nitrogens 1, 3 and 9 come from the ammonia pool;[18] carbons 2 and 8 are derived from formate;[19–21] carbon 6 comes from CO_2[20, 21] and carbons 4 and 5 and nitrogen 7 come from glycine.[20, 21] Steps of this nature (not necessarily from the same precursors) must occur in all organisms without an exogenous purine requirement. That these reactions are blocked in

Tetrahymena is shown by the requirement for guanine and the sparing action of adenine. Reaction 3 probably takes place in Tetrahymena. It may also take place in the four guanine-less mutants of the ascomycete Ophiostoma reported by Fries.[22,23] This reaction is blocked in the rat, as it was found that the administration of isotopically labeled guanine did not lead to the appearance of the isotope in the tissue purines.[24,25] Reaction 4 is blocked in Tetrahymena but may take place in the rat. Reaction 5 may take place in Tetrahymena but probably does not take place in the mammal, for if it did, in view of the apparent wide-spread ability of many or all organisms to aminate hypoxanthine to adenine, then dietary guanine would be converted to adenine via hypoxanthine. This appears to be precluded by the results of the tracer studies. Guanase activity occurs in the rat, but

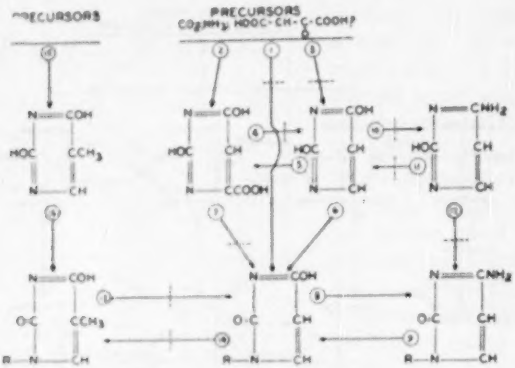

FIGURE 4

Schematic representation of the metabolism of pyrimidines. The dotted lines represent blocks in specific enzyme systems which occur in Tetrahymena. For evidence see text.

the result is xanthine, not hypoxanthine. Reaction 6 is blocked in Tetrahymena and the Ophiostoma mutants as evidenced by the fact that hypoxanthine will not replace guanine. Nothing is known about a xanthine oxidase (reactions 7 and 8) in Tetrahymena, although these are well-recognized reactions in many forms.

Reaction 9 is known to occur in Tetrahymena and the guanine-less Ophiotoma mutants[22,23] but it probably does not occur in the rat, while reactions 10 and 11 certainly do occur in the mammal and reaction 10, at least, occurs in Tetrahymena. Reaction 12 takes place in Tetrahymena, and may also take place in the rat, while reaction 13 is blocked in Tetrahymena as shown by the fact that adenosine and adenylic acid are incapable of replacing guanine while guanosine and guanylic acid are fully active.[1] Reac-

tion 14 is not known to occur in Tetrahymena, but, inasmuch as inosinic acid will not meet the guanine requirement, reaction 15 is certainly blocked. Reactions 16 and 17 are known to occur in many organisms and probably take place in Tetrahymena, as indicated by the different results obtained when hypoxanthine and adenine inhibitors were employed.

Figure 4 is a summary of the various steps in the metabolism of pyrimidines. Inasmuch as Mitchell, *et al.*,[9,10] have shown that certain pyrimidineless Neurospora mutants can use non-pyrimidine compounds and have suggested that ring closure does not precede the riboside linkage, we may suppose that at least three alternate routes of pyrimidine nucleoside synthesis developed in pre-animal systems. The first (reaction 1) is illustrated by the Neurospora mutants,[9,10] where it appears that oxaloacetic acid is converted to amino-fumaric acid and the riboside linkage completed before the pyrimidine ring is closed to form uridine. Whether these reactions are utilized to some degree in the rat is not known, but it is known that nitrogens 1 and 3 of the pyrimidine ring are derived from the ammonia pool[18] while carbon 2 is derived from CO_2.[21] It seems clear from the tracer studies of Arvidson, *et. al.*,[12] that orotic acid is utilized in the synthesis of uridine and is therefore synthesized from non-pyrimidine precursors (reaction 2). The interpretation placed upon these observations by Arvidson, *et al.*, was that orotic acid was linked with the sugar to form orotic nucleoside and then decarboxylated to uridine. Reactions 1 and 7 are blocked in Tetrahymena as is also probable for reaction 2. It is also clear that reaction 3 is blocked in this organism, which leaves preformed uracil as a required compound. Reaction 4 is blocked in Tetrahymena, while reaction 5 is blocked in the rat.[24] Reaction 6 is blocked in the rat,[24] but this reaction (sugar linkage to uracil) is very efficient in Tetrahymena, as evidenced by the fact that uracil and uridine are of approximately equal activity on a molar basis.[3] Reductive amination of uridine and oxidative deamination of cytidine (reactions 8 and 9) appear to be carried out with ease in many organisms[25, 27, 28] and Tetrahymena is no exception. Reactions 10, 11 and 12 are blocked in Tetrahymena as they appear to be likewise blocked in Neurospora mutants,[27, 28] Ophiostoma mutants[22, 23] and in the rat.[26] The fact that cytosine does not replace or spare uracil for Tetrahymena denotes blocks in reactions 11 and 12, while block 10 is inferred from the fact that uracil is as active as uridine on a molar basis. This would hardly be the case if part of the uracil were being sacrificed to produce an inert compound.

As has been stated, thymine is inactive for uracil replacement and sparing,[3] so there appears to be no methylation of uracil to thymine. Likewise thymidine will not replace nor spare uracil, which denotes blocks in reactions 13 and 14. Since large quantities of desoxyribose nucleic acid are present in these cells, it seems probable that thymine must be synthesized

from non-pyrimidine precursors (reactions 15 and 16). Both reactions 15 and 16 appear to depend upon pteroylglutamic acid, because thymine and thymidine are active in sparing this compound.

Recently Reichard[28] has presented evidence which indicates that thymine is derived from orotic acid in the rat. Administration of N^{15} labeled orotic acid resulted in the isotope appearing in low concentrations in the cytosine and thymine isolated from the tissue desoxyribose nucleic acid. If the purity of the isolated pyrimidines was satisfactory, this is a significant finding and would indicate that the rat has enzymes capable of methylating position 5 of orotic acid and/or orotic acid riboside and/or uridine.

Summary.—The animal microorganism, Tetrahymena, cannot synthesize the imidazole ring as evidenced by the failure of 2,4-diamino-5-formylamino-6-hydroxy pyrimidine to replace guanine. The triazolo analog of adenine (adenazolo) is inhibitory, with an inhibition index of 5. This inhibition is not released by any purine tested except adenine. Orotic acid is inactive for Tetrahymena, indicating a lack of specific decarboxylating enzymes. Evidence for the synthesis of thymine from non-pyrimidine precursors is presented. The synthesis of thymine and the formation of its desoxyriboside appear to be PGA controlled. Thymidine is approximately twice as active in sparing PGA as is thymine. Comparative enzymatic capacities for purine and pyrimidine metabolism are discussed.

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PARTIAL ORDERING IN THEORY OF STOCHASTIC PROCESSES

BY S. BOCHNER

DEPARTMENT OF MATHEMATICS, PRINCETON UNIVERSITY

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We take a directed set $\{\alpha\}$, so that $\alpha < \alpha$, $\alpha < \beta$ and $\beta < \gamma$ implies $\alpha < \gamma$, and to any α and β there is a γ such that $\alpha < \gamma$ and $\beta < \gamma$; and we consider a family of spaces $\{R_\alpha\}$ indexed by it, and for any $\alpha < \beta$ a map $x_\alpha = \varphi_{\alpha\beta}x_\beta$ from R_β onto all of R_α, also called projection, such that for $\alpha < \beta < \gamma$ we have $\varphi_{\alpha\beta}\varphi_{\beta\gamma} = \varphi_{\alpha\gamma}$ ("consistency"). In the direct product of all spaces R_α there is a "diagonal" set $\{x_\alpha\}$ in which $x_\alpha = \varphi_{\alpha\beta}x_\beta$ for $\alpha < \beta$ and this is the so-called projective limit of the given inverse mapping system.[1] The limit will be denoted by R or more explicitly by R_∞, and we note that each point x_α of every R_α is the α-th component of at least one point in R. The space could, but will not be appended to the given family by putting $\alpha < \infty$, $x_\infty = \varphi_{\alpha\infty}^{-1}(\{x_\beta\})$.

We denote by A_α a set of subsets of each R_α, such that for $S_\alpha \in A_\alpha$ and $\alpha < \beta$ we have $\varphi_{\alpha\beta}^{-1}(S_\alpha) \in A_\beta$. Each $\varphi_{\alpha\infty}^{-1}(S_\alpha)$ is a subset of R and the set of the latter subsets will be denoted by A or A_∞. If each A_α is a Boolean algebra then so is A itself, but if they are σ-algebras then A need no longer be one. We assume that on each algebra A_α there is given a finitely additive measure m_α, so that $m_\alpha R_\alpha = 1$, and that they are consistent, $m_\beta[\varphi_{\alpha\beta}^{-1}(S_\alpha)] = m_\alpha S_\alpha$. This gives rise to a such-like measure mS on A, $m[\varphi_{\alpha\infty}^{-1}(S_\alpha)] = m_\alpha S_\alpha$, but σ-additivity need no longer reproduce itself. However the following theorem can be stated which for

ordinary sequences of Euclidean spaces was first given by A. Kolmogoroff,[2] and for directed sets of Euclidean spaces in a previous paper of ours.[3]

THEOREM 1. *If each R_α is a Hausdorff space, and the given σ-measures m_α are such that for any S_α and any $\epsilon > 0$ there exists a compact subset F_α of S_α such that $m_\alpha F_\alpha > m_\alpha S_\alpha - \epsilon$; then the limit measure mS is σ-additive on a σ-closure of A.*

Proof: R itself is also a Hausdorff space,[1] and if F_α is compact in R_α then $\varphi_{\alpha\infty}^{-1}(F_\alpha)$ is compact in R. Therefore, to any S in A and any $\epsilon > 0$ there exists a compact subset F of S such that $mF > mS - \epsilon$.

Now, by a general criterion, a finitely additive measure in S has a σ-extension if $S^1 \supset S^2 \supset \ldots \to 0$ implies $mS^n \to 0$. If it is not fulfilled, there exists a sequence $\{S^n\}$, with $\lim S^n = 0$ and $mS^n \geq 2m_0 > 0$. But then we could find compact subsets F^n of S^n such that $m(S^n - F^n) \leq m_0 2^{-n}$. The intersections $G^n = \Pi_{j=1}^{n} F^j$ would still be compact subsets of S^n, and $m(S^n - G^n) \leq m_0$. Therefore $mG^n \geq m_0$, and no G^n is empty. But $G^n \supset G^{n+1}$, and thus the set-limit of G^n could not be empty, contrary to the tentative assumption that the set limit of S^n so was. q. e. d.

As an application consider on any space M an arbitrary (non-continuous) path $x(t)$, $a < t < b$, a and b fixed finite or infinite. The index α shall be any selection of time points $\alpha = (t_0, t_1, \ldots, t_n)$, $t_0 < t_1 < \ldots < t_n$; and if $\beta = (\tau_0, \tau_1, \ldots, \tau_m)$ then put $\alpha < \beta$ if and only if $n \leq m$ and each t_ν equals some τ_μ. For given α the space R_α shall be the $(n+1)$-fold product $Mx \ldots xM$, A_α shall be a suitable algebra of subsets, and $m_\alpha(S_\alpha)$, $S_\alpha \in A_\alpha$, shall be an *a priori* probability for the $n+1$ points $y(t_0), \ldots, y(t_n)$ on the arbitrary path in M to be lying in S_α. And these *a priori* probabilities shall be "consistent" with each other in the manner previously stipulated. The conclusion from Theorem 1 is then as follows. If M has a topological Hausdorff structure, if we transmit this structure to R_α, and if the measurable sets S_α are Borel sets in the topology of R_α, then the assemblage of all arbitrary paths in M can be made into a stochastic process by introducing into it a probability measure of which the given *a priori* probabilities are the natural projections.

If we put $t_0 =$ constant, and correspondingly $x(t_0) =$ constant (all paths emanating from the same point), then R_α is an n-fold manifold, the theorem again applies, and the resulting stochastic process is a so-called Brownian motion. Furthermore, if we consider discrete time-points, $t_\nu = \nu h$, it suffices to consider indices α with only consecutive time elements, $\alpha = (0, h, 2h, \ldots, nh)$, and if the space M is the real line in the natural topology (or perhaps the complex plane) then the set-up is the classical case of a sequence of random variables $(x_0), x_1, x_2, \ldots$; and if there are given consistent joint distributions for say $x_1, \ldots, x_n$, $n = 1, 2, 3, \ldots$ then by Theorem 1 the infinite sequence can be made into a stochastic process, and this is the known theorem of Cantelli and Kolmogoroff.

This Euclidean situation was treated previously in a rather comprehensive manner.[3]

Next, consider on M a (finite or infinite) Lebesgue volume in which Borel sets are measurable, and relative to it in $0 < t < \infty$ a Markoff density $f(r, x;\ s, y)$, $r < s$, with the known properties

$$\int_M f(r, x;\ s, y)dv_y = 1, \qquad f \geq 0$$
$$\int_M f(r, x;\ s, y)f(s, y;\ t, z)dv_y = f(r, x;\ t, z).$$

It gives rise to a Brownian motion as previously introduced if we define $m_\alpha S_\alpha$ as

$$\int \ldots \int_S f(t_0, x_0;\ t_1, x_1)f(t_1, x_1;\ t_2, x_2) \ldots f(t_{n-1}, x_{n-1};\ t_n, x_n)dv_{x_1} \ldots dv_{x_n},$$

and if the Markoff chain is stationary, that is, $f(r, x;\ s, y) = f(s - r;\ x, y)$, then on introducing the lengths $r_1 = t_1 - t_0$, $r_2 = t_2 - t_1$, $\ldots$, this $m_\alpha S_\alpha$ is

$$\int \ldots \int_S f(r_1; x_0, x_1)f(r_2; x_1, x_2) \ldots f(r_n; x_{n-1}, x_n)dv_{x_1} \ldots dv_{x_n}. \qquad (1)$$

This stochastic process is built up of infinitesimal transitions which are stochastically independent, but we can relax this restrictive independence by the following device.

Take a set-up $\{R_\alpha;\ A_\alpha\}$ as before, and on it not only one (consistent) *a priori* probability $m_\alpha S_\alpha$ but a whole family of such probabilities $m_\alpha^{(\rho)} S_\alpha$. Then any linear combination

$$m_\alpha S_\alpha = \sum_\rho \gamma_\rho m_\alpha^{(\rho)} S_\alpha$$

with $\gamma_\rho \geq 0$, $\sum_\rho \gamma_\rho = 1$, and suitable limits of such combinations, are again admissible probabilities. In particular, if we are given a stationary Markoff chain $f(r; x, y)$ then for fixed $t > 0$, $f(tr; x, y)$ is again such a chain, and by the rule just stated we obtain a "brownian motion" if in equation (1) we replace the integrand by the more general integrand

$$\int_0^\infty f(tr_1; x_0, x_1)f(tr_2; x_1, x_2) \ldots f(tr_n; x_{n-1}, x_n)d\,\gamma(t)$$

where $\gamma(t)$ is monotone in $0 < t < \infty$ with $\gamma(+0) = 0$, $\gamma(\infty) = 1$.

This modification of one stochastic process into another by means of a positive integral transformation must be carefully distinguished from another one previously given[4] in which one Markoff chain is being modified into another Markoff chain by the following general procedure. Consider on M a stationary Markoff chain with a density $f(r; x, y)$, but assume that the time points $r, s, t, \ldots$ are elements of an arbitrary semigroup T in which a commutative associative addition $r + s$ is defined. We take another such general semigroup U with elements $u, v, w, \ldots$, and we assume that for $r \in T$, $u \in U$ we are given a real-valued function $\gamma(r; u)$ which is monotonely increasing on T, that is $\gamma(r + s; u) \geq \gamma(r; u)$, in

conjunction with a certain topology on T, so that for bounded continuous functions $h(r)$ and every u a Stieltjes integral

$$\int_T h(r)\, d\,\gamma(r; u)$$

shall be definable, and we assume that $\int_T d\,\gamma(r; u) = 1$ and

$$\int_{r+s=t} d\,\gamma(r; u)\, d\,\gamma(s; v) = d\,\gamma(t; u+v).$$

If now we introduce the function

$$g(u; x, y) = \int_T f(r; x, y)\, d\,\gamma(r; u) \tag{2}$$

then it has again all properties of a stationary Markoff chain and this is the transformation we wanted to describe. In particular if both T and U are the half line $(0, \infty)$ as usual, then a "matrix" $\{d\,\gamma(r, u)\}$ with the stated properties will be obtained from the Laplace Stieltjes expansion

$$\exp[-u\Phi(\lambda)] = \int_0^\infty e^{-\lambda t} d\,\gamma(t; u)$$

if $\Phi(\lambda)$ is any continuous function in $0 \leq \lambda < \infty$ with $\Phi(0) = 0$ for which such an expansion is available for $u > 0$. For instance, $\Phi(\lambda) = \lambda^\rho$, $0 < \rho < 1$, is of this kind.

But now take a set of functions $\Phi_p(\lambda)$, $p = 1, 2, \ldots$, of the kind just introduced, and for fixed k associate with them linear forms $L_p(u) = \gamma_{p1}u_1 + \ldots + \gamma_{pk}u_k$ with real coefficients γ_{pj}. If now we introduce in the space of k-dimensional vectors $u = (u_1, \ldots, u_k)$ the convex cone U which is defined by $L_p(u) > 0$, $p = 1, 2, \ldots$, then for u in U we again have an expansion

$$\exp[-\textstyle\sum_p L_p(u)\Phi_p(\gamma)] = \int_0^\infty e^{-\lambda t}\, d\,\gamma(t; u).$$

If we take any unitemporal chain $f(r; x, y)$ and make the transformation (2) then the resulting process $g(r; x, y)$ is more or less what P. Lévy has been lately calling a multiple Markoff chain. If in particular we start with

$$f(r; x, y) = \textstyle\sum_n e^{-r\lambda_n}\varphi_n(x)\varphi_n(y)$$

where $\{\lambda_n; \varphi_n\}$ are the eigenvalues and the eigenfunctions of a Laplacean $-\Delta$ on a compact Riemann space[4] then we have

$$g(u; x, y) = \textstyle\sum_n \exp[-\sum_p L_p(u)\Phi_p(\lambda_n)]\varphi_n(x)\varphi_n(y),$$

and if we put $\sum_p L_p(u)\Phi_p(\lambda) = \sum_{j=1}^k u_j\Psi_j(\lambda)$, that is $\Psi_j(\lambda) = \sum_p \gamma_{pj}\Phi_p(\lambda)$, then the system of diffusion equations

$$-\frac{\partial g(u; x, y)}{\partial u_j} = \Psi_j(-\Delta_x)g(u; x, y), \qquad j = 1, \ldots, k$$

is satisfied, and this is a generalization of the Fokker-Planck equations

from unitemporal to multitemporal processes. A significant interpretation of multitemporal processes from the vantage point of such systems of equations would be indicated.

[1] See Lefschetz, S., *Algebraic Topology*, 1942, p. 31; and Braconnier, Jean, "Spectres d'espaces et de groupes topologiques," *Portugaliae Math.*, **1**, 93–111 (1948).

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COHOMOLOGY THEORY OF ABELIAN GROUPS AND HOMOTOPY THEORY I

BY SAMUEL EILENBERG AND SAUNDERS MACLANE*

DEPARTMENTS OF MATHEMATICS, COLUMBIA UNIVERSITY AND THE UNIVERSITY OF CHICAGO

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If a topological space X is aspherical (i.e., if all homotopy groups other than the fundamental group vanish), Hurewicz has shown that the fundamental group π_1 of the space determines all the homology and cohomology groups of the space. After further investigations by H. Hopf, the authors and subsequently others[1] obtained an algebraic formulation for this determination, by exhibiting, for each abelian coefficient group G, a natural isomorphism

$$H^k(X; G) \cong H^k(\pi_1; G), \qquad k = 1, 2, \ldots \tag{1}$$

between any cohomology group of the space and the corresponding (algebraic) cohomology group of the group π_1. The latter groups are defined as the cohomology groups of a certain cell complex $K = K(\pi_1, 1)$ depending only on the group π_1. The q-dimensional cells of this complex are all the q-tuples $[x_1, \ldots, x_q]$ of elements x_i of the group, and for $q > 1$ the boundary of any such cell is defined as

$$\partial[x_1, \ldots, x_q] = [x_2, \ldots, x_q] + \sum_{i=1}^{q-1} (-1)^i [x_1, \ldots, x_i x_{i+1}, \ldots, x_q] + (-1)^q [x_1, \ldots, x_{q-1}]. \tag{2}$$

A "normalization" of this complex is also possible. If K_N is the subcomplex spanned by all cells $[x_1, \ldots, x_q]$ with some $x_i = 1$, then the cohomology groups $H^k(\pi_1; G)$ of K are isomorphic[2] to the relative groups of K modulo K_N.

In the study of the effect of higher homotopy groups upon cohomology (and homology) groups, it appears efficient to first isolate the effect of a single homotopy group. Hence, in this note we consider any arcwise connected topological space X, in which the mth (abelian) homotopy group $\Pi = \pi_m$ is given, with $m > 1$, and in which all the other homotopy groups vanish ($\pi_1 = 1$, $\pi_i = 0$ for $i \neq 1, i \neq m$). Previously, we obtained,[3] in analogy with (1), an expression

$$H^k(X; G) \cong H^k[K(\Pi, m);\ G] \qquad k = 1, 2, \ldots \tag{3}$$

for the singular cohomology groups of the space in terms of the cohomology groups of a certain cell complex $K(\Pi, m)$ defined algebraically in a fashion similar to $K(\Pi, 1)$, but depending essentially upon the commutativity of Π (see the detailed description below).

The algebraic cohomology groups appearing in (1) and (3) are also essential for the definition[4] of certain "obstruction invariants" of spaces; these in turn, seem to be applicable to the problem of extension and classification of continuous mappings.[5] In a very few cases, the groups of $K(\Pi, m)$ have been computed[6] by applying deeper methods of homotopy theory to a suitably constructed topological space.

This note will state some of the results of a systematic study of the groups of $K(\Pi, m)$ by purely algebraic methods. A main result is the fact that these groups obey a curious analog of the Freudenthal suspension theorem.[7]

We begin with a description of the complex $K(\Pi, m)$. Choose for each positive integer q a standard q-dimensional simplex Δ_q with ordered vertices $(0, 1, \ldots, q)$, and let e_q^i, for $i = 0, 1, \ldots, q$, denote that mapping of Δ_{q-1} in Δ_q obtained by mapping the vertices $0, 1, \ldots, q-1$ of Δ_{q-1} in order upon the vertices of Δ_q, omitting the vertex i of Δ_q. The q-cells of the complex $K(\Pi, m)$ are the m-dimensional cocycles $g \in Z^m(\Delta_q; \Pi)$; for each g, the mapping e_q^i yields a cocycle $F_i g = g e_q^i \in Z^m(\Delta_{q-1}; \Pi)$, and thus a $q-1$ cell of K. The boundary of the q-cell g is defined as $\partial g = \sum (-1)^i F_i g$, where the addition from $i = 0$ to q is to be regarded as a sum of cells (and not as addition of cocycles). $K(\Pi, m)$ is the cell complex with these cells and this boundary formula.

The suspension homomorphism, mapping $K(\Pi, m)$ into $K(\Pi, m+1)$, is obtained by first assigning, to each g, the "suspended" $(m+1)$ cocycle Tg on Δ_{q+1}, defined for each $m+1$ dimensional ordered simplex $(r_0, \ldots, r_{m+1})$ of Δ_{q+1} as

$$\begin{aligned} (Tg)(r_0, \ldots, r_{m+1}) &= g(r_0, \ldots, r_m) && \text{if } r_{m+1} = q+1, \\ &= 0 && \text{if } r_{m+1} < q+1. \end{aligned}$$

If g_0 denotes the cocycle which is identically zero, in the appropriate dimension, then the suspension mapping

$$Sg = Tg - g_0 \tag{4}$$

is a chain transformation (raising dimensions by 1) of $K(\Pi, m)$ into $K(\Pi, m+1)$, and hence induces homomorphisms

$$S: H^{m+k}[K(\Pi, m+1);\ G] \to H^{m-1+k}[K(\Pi, m);\ G] \tag{5}$$

on the corresponding cohomology groups, for $k = 1, 2, \ldots$.

THEOREM 1. *For $k \leqq m$, the suspension homomorphism S is an isomorphism onto. For $k = m+1$, it is an isomorphism into.*

The argument depends upon an algebraic reduction of the complex $K(\Pi, m)$ to a simpler "cubical" complex $Q(\Pi)$ depending on the abelian group Π alone. Each element x of Π determines a 1-cell $[x]$ of Q, each pair x, y, a 2-cell $[x, y]$ of Q, with boundary

$$\partial[x, y] = [x] + [y] - [x + y]. \tag{6}$$

A 3-cell of Q is a 2×2 square of elements in Π, with boundary

$$\partial\begin{bmatrix} x & y \\ r & s \end{bmatrix} = [x, y] + [r, s] - [x + r, y + s] - [x, r] - [y, s] + [x + y, r + s]. \tag{7}$$

The proof that $\partial\partial = 0$ uses the hypothesis that Π is abelian.

In general, an $(n+1)$-cell of Q will be a $2 \times 2 \times \cdots \times 2$ hypercube of dimension n, with entries in Π, and the boundary will consist of $3n$ terms formed, as in (7), by slicing the hypercube. Explicitly, label the vertices of the hypercube by the n-tuples $(\epsilon_1, \ldots, \epsilon_n)$ with each $\epsilon_i = 0$ or 1. An $(n+1)$-cell of Q is any function σ with arguments all n-tuples $(\epsilon_1, \ldots, \epsilon_n)$ and with values in Π. The faces R_i, S_i, and P_i of σ are defined, for $i = 1, \ldots, n$, to be the n-cells

$$\begin{aligned}
(R_i\sigma)(\epsilon_1, \ldots, \epsilon_{n-1}) &= \sigma(\epsilon_1, \ldots, \epsilon_{i-1}, 0, \epsilon_i, \ldots, \epsilon_{n-1}), \\
(S_i\sigma)(\epsilon_1, \ldots, \epsilon_{n-1}) &= \sigma(\epsilon_1, \ldots, \epsilon_{i-1}, 1, \epsilon_i, \ldots, \epsilon_{n-1}), \\
(P_i\sigma)(\epsilon_1, \ldots, \epsilon_{n-1}) &= (R_i\sigma)(\epsilon_1, \ldots, \epsilon_{n-1}) + (S_i\sigma)(\epsilon_1, \ldots, \epsilon_{n-1}),
\end{aligned}$$

where the addition is that of the group Π. The boundary of σ is

$$\partial\sigma = \sum_{i=1}^{n} (-1)^i (P_i\sigma - R_i\sigma - S_i\sigma)$$

where the addition is that of chains in Q; one has $\partial\partial = 0$.

Within the complex Q consider the subcomplex Q_N which is spanned by the "slabs" (all those $n+1$ cells σ with $n \geqq 1$ such that for some index i one has either $R_i\sigma$ or $S_i\sigma$ identically zero) and by the "diagonals" (all those cells of the form $D_i\sigma$ for some i), where

$$(D_i\sigma)(\epsilon_1, \ldots, \epsilon_{n+1}) = \sigma(\epsilon_1, \ldots, \epsilon_i, \epsilon_{i+2}, \ldots, \epsilon_{n+1}), \quad \epsilon_i = \epsilon_{i+1},$$
$$= 0 \quad \text{if} \quad \epsilon_i \neq \epsilon_{i+1}.$$

For any abelian group G we then define the *cubical cohomology groups* $Q^n(\Pi; G)$ as the relative cohomology groups of Q modulo Q_N;

$$Q^n(\Pi; G) = H^n(Q, Q_N; G). \tag{8}$$

In particular, equation (6) shows that a 1-dimensional cubical cocycle is a homomorphism, so that $Q^1(\Pi; G)$ is the group of homomorphisms of Π into G. Similarly equation (7) implies that a 2-dimensional cubical cocycle is a (normalized) symmetric factor set $f(x, y)$ of Π in G, so that $Q^2(\Pi; G)$ is the group of abelian group extensions[8] of G by Π. The higher cubical cohomology groups of Π appear to be new.

THEOREM 2. *If $\Pi + \Pi'$ is the direct sum of two abelian groups, there is a natural isomorphism*

$$Q^n(\Pi + \Pi'; G) \cong Q^n(\Pi; G) + Q^n(\Pi'; G).$$

In a subsequent note we shall show that this property, together with the character of the complex Q in the case when Π is an infinite cyclic semigroup, serve to characterize the cubical cohomology groups, in the sense that any other construction for all groups Π of suitable cell complexes with these properties yields exactly the cubical cohomology groups here defined.

THEOREM 3. *There are isomorphisms*

$$H^{m-1+k}[K(\Pi, m); G] \cong Q^k(\Pi; G), \qquad k = 1, 2, \ldots, m.$$

The isomorphism θ in question is related to the suspension homomorphism S by $\theta S = \theta$; hence this result at once yields the suspension theorem, for $k \leqq m$.

To extend this result to higher values of k, we introduce a sequence of cohomology groups intermediate to the cubical and the ordinary cohomology groups of Π. They are defined by means of subcomplexes Q_t of Q, for $t = 0, 1, 2, \ldots, \infty$. Call an index $i (i = 1, \ldots, n-1)$ *critical* for an $(n+1)$-cell σ if $R_iS_i\sigma$ is not identically zero; that is, if $\sigma(\epsilon_1, \ldots, \epsilon_{i-1}, 1, 0, \epsilon_{i+2}, \ldots, \epsilon_n) \neq 0$ for some choice of the ϵ's. The *level* of a cell σ is the number of distinct critical indices for σ. The complex $Q_t(\Pi)$ is defined as that subcomplex of $Q(\Pi)$ which is spanned by all cells of level at most t. In particular, if $n \leqq t+1$, any $(n+1)$-cell σ lies in Q_t. We define the cubical cohomology groups of level t for Π as the relative groups of Q_t modulo $Q_t \cap Q_N$:

$$Q^{n,t}(\Pi; G) = H^n(Q_t, Q_t \cap Q_N; G). \tag{9}$$

The complex Q_∞ is the whole complex Q, hence $Q^{n,\infty}(\Pi) = Q^n(\Pi)$, and also $Q^{n,t}(\Pi) = Q^n(\Pi)$, if $n \leqq t+1$. On the other hand, the $(n+1)$-

cells of Q_0 have $\sigma(\epsilon_1, \ldots, \epsilon_n) = 0$, unless $\epsilon_1 \leqq \epsilon_2 \leqq \ldots \leqq \epsilon_n$, hence may be mapped in 1-1 fashion on the $(n + 1)$ tuples $[x_1, \ldots, x_{n+1}]$, where $x_i = \sigma(0, 0, \ldots, 0, 1, \ldots, 1)$ with i-1 arguments equal to 1. This correspondence can be used to show that $Q^{n,0}(\Pi; G)$ is the nth cohomology group of $K(\Pi, 1)$, modulo K_N; hence

$$Q^{n,0}(\Pi; G) \cong H^n(\Pi; G). \tag{10}$$

Theorem 3 may now be extended as follows.

THEOREM 4. *For all $k = 1, 2, \ldots$ there is an isomorphism*

$$H^{m-1+k}[K(\Pi, m); G] \cong Q^{k,m-1}(\Pi; G).$$

In view of (3), we thus have

THEOREM 5. *If X is an arcwise connected topological space with a given homotopy group π_m and with all other homotopy groups trivial, the singular cohomology groups of X with coefficients in any abelian group G are determined by π_m according to the formulae*

$$H^q(X; G) = 0, \qquad q = 1, 2, \ldots, m - 1,$$
$$H^{m-1+k}(X; G) = Q^{k,m-1}(\pi_m; G), \qquad k = 1, 2, \ldots.$$

The theorem formally includes the case $m = 1$. Briefly, we may say that the ordinary cohomology groups for the *not* necessarily *abelian* fundamental group yield the effect of that group upon cohomology groups of the space, and that the cubical cohomology groups, defined, at suitable levels, for *abelian* groups, provide the corresponding effect for higher homotopy groups.

In a later note we shall give an alternative description of the groups $Q^{k,m-1}(\Pi; G)$ which is more suitable for algebraic computations and topological applications.

* Essential portions of the study here summarized were done during the tenure of a John Simon Guggenheim Memorial Fellowship by one of the authors.

[1] The literature is summarized in Eilenberg, S., *Bull. Am. Math. Soc.*, **55**, 3–37 (1949).

[2] Eilenberg, S., and MacLane, S., *Ann. Math.*, **48**, 51–78 (1947).

[3] Eilenberg, S., and MacLane, S., *Ibid.*, **46**, 480–509 (1945).

[4] Eilenberg, S., and MacLane, S., "Relations between Homology and Homotopy Groups of Spaces, II," *Ibid.*, to appear.

[5] Whitney, H., *Ibid.*, **50**, 285–296 (1949).

[6] Whitehead, G. W., PROC. NATL. ACAD. SCI., **34**, 207–211 (1948).

[7] Freudenthal, H., *Compositio Math.*, **5**, 299–314 (1937).

[8] This is the group Ext (G, π) used in Eilenberg and MacLane, *Ann. Math.*, **43**, 757–831 (1942).

REMARKS ON THE COMPARISON OF AXIOM SYSTEMS

BY HAO WANG

SOCIETY OF FELLOWS, HARVARD UNIVERSITY

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With the arithmetization of syntax, we can formulate the metalogical problems of consistency, completeness, decidability, relative consistency, etc., as arithmetic problems. On certain occasions this kind of formulation can render the crucial notions more exact. In this note we shall assume that the syntax of each of the systems we consider is arithmetized, and talk in terms of the arithmetic propositions expressing the syntactic properties. In particular, the arithmetic proposition Con(S) expresses the consistency of S. We shall make a few observations on the comparison of systems according to the following three standards (S and S' being two systems): (1) whether Con(S) is provable in S'; (2) whether S is translatable into S'; (3) whether we can obtain in S' a Tarski truth function (or set) for S.

We propose first a few definitions.[1]

Definition 1: A system S is said to be translatable into or obtainable within or contained as a part in a system S' if there exists a general recursive function T mapping the set of the numbers representing (via the arithmetization) the propositions of S into the set of the numbers representing those of S' such that the set of (the numbers representing) the theorems of S is mapped into the set of those of S' and the image of the negation of a proposition of S is the negation of the image of the proposition.

We note that a function maps the set of the theorems of S into that of S' if and only if axioms of S all correspond to theorems of S' and primitive rules of inference of S all correspond to valid rules of inference of S'. If we assume that systems for various branches of mathematics are given to start with, then the above definition provides us with a more precise meaning to the oft-repeated assertion that mathematics is reducible to or obtainable in logic (that is to say, in certain forms of set theory).

Definition 2: Two systems S and S' are said to be of equal strength if the propositions Con(S) and Con(S') are mutually derivable in number theory. S' is said to be stronger than S if Con(S) is derivable from Con(S') in number theory but not conversely.

Definition 3: A system which contains number theory as a part is said to be a mathematical system. (In particular, a system of number theory is a mathematical system.) If Con(S) is a theorem of number theory, then S is said to be an elementary system.

Using these definitions, we can prove the following theorems:

THEOREM 1. *If S is translatable into S', then Con(S) is derivable from Con(S') in number theory. If S and S' are translatable into each other, then*

they are of equal strength. If S is stronger than S', then S is not translatable into S'.

Proof: The translation of a proof of S that gives a contradiction is a proof of S' which also gives a contradiction, and vice versa.

THEOREM 2. *All consistent, decidable systems are elementary, and therefore of equal strength.*

Proof: Following a by now established usage, we call a system S decidable if the class of its theorems is general recursive. Let S be a system which is both consistent and decidable. Since all general recursive functions are definable in number theory, there exists a function f for which we can prove in number theory either that $f(n)$ is 0 or that $f(n)$ is 1 according as n represents a theorem of S or not. But S is consistent. Hence, there is a number k which represents a proposition of S which is not a theorem. Therefore, we can prove in number theory that $f(k)$ is 1. Hence, the proposition Con(S) is a theorem of number theory.

Thus, from results of Post, Löwenheim, Presburger and Skolem, we know that propositional calculus, monadic restricted functional calculus, arithmetic with just addition and arithmetic with just multiplication are all elementary systems. However, not all elementary systems are decidable. One case is the restricted functional calculus which has been shown by Church to be undecidable. The usual proof for its consistency[2] amounts to showing that it is translatable into the propositional calculus. Hence, by Theorem 1, it is an elementary system, and we have:

THEOREM 3. *There exist elementary systems which are not decidable.*

According to a theorem of Gödel, if S is a mathematical system, then Con(S) is not a theorem of S (unless S is inconsistent). Hence, if Con(S) is a theorem of a mathematical system S', then Con(S') is not derivable from Con(S) in S' or in number theory (unless S' is inconsistent). On the other hand, if S' contains S as a part, by Theorem 1, Con(S) is derivable from Con(S') in number theory. Hence, we have:

THEOREM 4. *If S' is consistent and contains a mathematical system S as a part and Con(S) is a theorem of S', then S' is stronger than S.*

By extending somewhat a formulation[3] of the well-known theorem on denumerable models (Löwenheim-Skolem-Herbrand-Gödel), we can prove the following theorem:

THEOREM 5. *Every system S is translatable into the system obtained from number theory by adding Con(S) as a new axiom.*

Let L be a system of set theory with finitely many special axioms such that number theory as well as a theory of the classes of natural numbers can be obtained in it.[4] Suppose x, y, z, etc., are the variables of L (or the variables of the highest type in L). Let L^n be a system related to L as a functional calculus of order n is related to one of order $n-1$, with the new variables X, Y, etc., and L' be the system which is like L^n except that the

new variables are not allowed in the definitions of classes of lower types. Thus, both L' and L'' contain a principle stating that for every propositional function (it may contain bound variables of the type just introduced) ϕx, there exists a class Y such that x belongs to Y if and only if ϕx. But L'' contains in addition also principles such as: for every propositional function of L'', there exists a class c (of a type in L) defined by it. Let further $L\sharp$ be the system obtained from L by adding Con(L) as a new axiom. We want now to consider the interrelationships among the systems L, L', L'' and $L\sharp$.

We observe first that with the methods developed by Tarski and others, we can give a truth set for L in L'' and prove Con(L) in L''. Moreover, since Con(L) is a theorem of L'', we can prove in L'' that the number representing the proposition Con(L) also belongs to the truth set so that Con($L\sharp$) is also a theorem of L''.

THEOREM 6. *Both Con(L) and Con($L\sharp$) are theorems of L''. Hence, L'' is stronger than $L\sharp$.*

By applying Theorem 5, we can prove that the mathematical system L' is translatable into $L\sharp$. Hence, we have:

THEOREM 7. *The proposition Con(L') is derivable from Con($L\sharp$) in number theory.*

It follows that Con($L\sharp$) is not provable in L' unless L' is inconsistent. Let us examine now why we cannot prove Con($L\sharp$) in L'.

It is not hard to obtain within L' a Tarski truth set for both L and $L\sharp$. Thus, let P_m be the propositional function represented by the number m. We want to prove:

THEOREM 8. *There exists a class Tr in L' such that for every given proposition P_m of L and $L\sharp$, we can prove in L' a theorem of the form (S): $m \in Tr$ if and only if P_m.*

The proof may be outlined as follows. For brevity, let us assume that L contains only one kind of variable x, y, etc., which may be written alternatively as v_1, v_2, etc. Following Professor W. V. Quine, we shall identify the infinite sequences of classes of L with the classes x of L such that x is a class of ordered pairs whose second terms are all positive integers. Let us use the letter g as a variable ranging over such classes of L. Then we can define the jth term g_j of an infinite sequence g, and the infinite sequence $t(g, n, y)$ obtained from g by substituting the class y for g_n. With these notions we can define a propositional function $R(k, X)$ of L' as follows: For all g and m, a pair $g;m$ belongs to X if and only if P_m is a propositional function of L containing no more than k logical operators and is such that either (1) P_m is $v_n \in v_j$ and $g_n \in g_j$, or (2) P_m is $P_n \downarrow P_j$ (neither P_n nor P_j) and $g;n \in X \downarrow g;j \in X$, or (3) P_m is $(v_n)P_j$ and $(y)(t(g, n, y);j \in X)$. Then Tr is just the class of natural numbers m such that $(g)(\exists X)(g;m \in X$ and $R(m, X))$. But for each given number m, we can

prove in L' the propositions: (1) $(EX)R(m, X)$; (2) for all Y and Z, if $R(m, Y)$ and $R(m, Z)$, then $Y = Z$. Therefore, we can prove in L' all the special cases falling under the schema (S).[5]

If we can prove in L' also that all theorems of L belong to Tr, then we can easily prove $\mathrm{Con}(L)$ in L'. Let us assume that the proofs of the theorems of L are enumerated in some way so that each proof is either (1) an axiom of one of the finitely many kinds of axioms of the restricted functional calculus, or (2) one of the finitely many special axioms of L, or (3) the result obtained from one or two previous proofs by adding one line in accordance with the ordinary rule of generalization or that of modus ponens. Let $b(n, m)$ be the proposition of L' stating that the nth proof in the above enumeration is a proof of P_m, and k be the number of the proposition $0 \neq 0$ of L. Then we can prove easily in L' the propositions (1) k does not belong to Tr, and (2) if $b(1, k)$ then k belongs to Tr. Moreover, since L contains only a finite number of special axioms, we can also prove in L' the following proposition: $(i)((n)((n \leqq i \text{ and } b(n, k)) \supset k \in Tr) \supset (b(i + 1, k) \supset k \in Tr))$. By combining this with the last two theorems of L', we can prove in L': $\sim b(1, k)$ and $(i)((n)(n \leqq i \supset \sim b(n, k)) \supset \sim b(i + 1, k))$. However, it does not follow that we can also prove in L' the proposition $(m) \sim b(m, k)$ which is equivalent to the proposition $\mathrm{Con}(L)$. In order to make the inference, we have to apply the induction principle saying that every class X (in L') of natural numbers has a least member. Since L contains number theory, we know that every class x (in L) has a least member. But we cannot infer that every class X (in L') of natural numbers also has a least number, unless we should assume (as in L'') that large variables are allowed in defining classes x, y, etc., and therefore every class X of natural numbers is identical with a class x of natural numbers.

Indeed,[6] if we could make the inference and prove $\mathrm{Con}(L)$ in L', $\mathrm{Con}(L\sharp)$ would also be a theorem of L' and L' would be inconsistent by Theorem 7. Thus, by the schema in Theorem 8, if $\mathrm{Con}(L)$ were a theorem of L', then we could prove in L' that the number representing $\mathrm{Con}(L)$ belongs to Tr, and therefore that all the numbers representing theorems of $L\sharp$ belong to Tr. Then it would follow immediately that $\mathrm{Con}(L\sharp)$ is a theorem of L'.

Since we assume in L number theory and a theory of classes of natural numbers, the number 0, the success or function $+1$, and the class Nn of natural numbers are all defined in L. In the arguments of the last two paragraphs we are assuming that these same definitions of L are also employed in L'. Let us now retain in L' the definitions of 0 and $+1$ used in L but redefine the class Nn as the intersection of all classes X such that 0 belongs to X and for every n, $n + 1$ belongs to X if n does. Then we can derive in L' the principle of induction for all classes of L' from the principle of class formation. Hence, we can prove in L' the arithmetic

proposition expressing the consistency of L. However, since the definition of the class of natural numbers in L' is different from that in L and $L\sharp$, the proposition we prove as a theorem in L' is different from the axiom of $L\sharp$ which also expresses the consistency of L. Therefore, although we can prove in L' a proposition $\mathrm{Con}(L)$ expressing the consistency of L, we cannot use the argument mentioned above to derive $\mathrm{Con}(L\sharp)$ in L'.

Summing up the last few paragraphs, we have:[7]

THEOREM 9. *If L' is consistent and we use in L' the same definitions of 0, $+1$, and Nn as in L and $L\sharp$, then (1) the principle of induction is independent of the axioms of L' and, in particular, there exists a propositional function $\phi(i)$ of L (viz., the propositional function $(n)(n \leqq i \supset \sim b(n, k))$) such that $\phi(0)$ and $(i)(\phi(i) \supset \phi(i+1))$ are provable in L' but $(m)\phi(m)$ is not; (2) although there is a truth set for L in L', $\mathrm{Con}(L)$ is not provable in L'.*

THEOREM 10. *By choosing suitable definitions for natural numbers, we can prove in L' the proposition $\mathrm{Con}(L)$. But $\mathrm{Con}(L\sharp)$ is not a theorem of L' unless L' is inconsistent.*

At several places Skolem stresses that the meaning of mathematical concepts (such as the concept of "natural number") is relative to the meaning of the concept of "set." The above two theorems seem to provide a rather remarkable illustration of Skolem's point.

We proceed to state a number of corollaries of the Theorems 1–10.

THEOREM 11. *$\mathrm{Con}(L')$ is a theorem of L''.*

Proof: By Theorem 6 and Theorem 7.

THEOREM 12. *L'' is stronger than L' and therefore not translatable into L'.*

Proof: By Theorem 11, Theorem 4 and Theorem 1.

THEOREM 13. *L' is stronger than L and therefore not translatable into L.*

Proof: By Theorem 10, Theorem 4 and Theorem 1.

THEOREM 14. *Although there is a truth set for $L\sharp$ in L', L' is translatable into $L\sharp$.*

Proof: By Theorem 8 and the proof of Theorem 7.

There seems to be a wide-spread impression that whenever we can obtain in a mathematical system S' a truth set for a system S, we can also prove $\mathrm{Con}(S)$ in S'. Since the proof of $\mathrm{Con}(S)$ depends more heavily on what axioms S contains than the definition of a truth set for S, there is not much reason to suppose that this should be true in general. And our results above provide us with a counter-example. Thus, by Theorem 8 and Theorem 10, we have:

THEOREM 15. *If L' is consistent, then $\mathrm{Con}(L\sharp)$ is not provable in L' although there is in L' a truth set for $L\sharp$.*

On the other hand, since a truth definition for L is also a truth definition for $L\sharp$, by Tarski's theorem stating that we cannot define truth of a mathematical system within the system itself, we have:

THEOREM 16. *Although Con(L) is a theorem of $L\phi$, we cannot obtain in $L\phi$ a truth definition for L.*

It is a pleasure to acknowledge here our indebtedness to Professors P. Bernays, W. V. Quine and J. B. Rosser for valuable suggestions and criticisms.

[1] Questions of equivalence and translatability among systems have been studied by numerous authors including R. Carnap (*Logical Syntax of Language*, London, 1937) and John G. Kemeny (*J. of Symbolic Logic*, **13**, 16–30 (1948); *Thesis*, Princeton University, 1949). The definitions we adopt in this note seem to differ from theirs considerably, probably because they are interested in more general problems. Many problems on the truth set *Tr* of a system have been treated carefully by A. Tarski in *Studia Philosophica*, **1**, 261–405 (1936).

Throughout this note, we shall mean by number theory a system which contains, beyond the restricted functional calculus and the theory of identity for natural numbers, the Peano axioms and the recursive equations for addition and multiplication.

The Definition 1 is quite liberal and for certain purposes, it may be desirable to add (as we have done at another place) a condition on the function T stating that the image of the conjunction of two propositions of S is the conjunction of their images. It will then follow that similar things hold for all the truth functions. Such a change in Definition 1 would not affect the proof of any of the theorems in this note.

Following a prevalent usage, we assume that the notions of proposition, axiom and immediate consequence in every *system* are all general recursive. In what follows, the translation of a proof will be understood as consisting of the translations of all the lines of the proof. It is not hard to see that if S is translatable into S' according to Definition 1, then there is a general recursive function mapping proofs in S onto their translations in S'.

[2] Hilbert and Ackermann, *Grundzüge der theoretischen Logik*, Berlin, 1938, p. 70.

[3] Hilbert and Bernays, *Grundlagen der Mathematik*, vol. 2, 1939, pp. 234–250. Details of proofs for theorems similar to the theorems 1, 5, 7, 8 and 10 of the present note are given in a longer paper of mine (entitled "On the Consistency Question of Analysis") which will probably be published in the future.

[4] For example, the system in Gödel, K., *The Consistency of the Continuum Hypothesis*, Princeton, 1940, or the alternative formulation given by the present author in these PROCEEDINGS, **35**, 150–155 (1949). We may take as L either the system determined by N1-N7 in that note or any subsystem of it containing roughly axioms answering to I–III, Va and VI in Bernays, P., *J. of Symbolic Logic*, **2**, 65–77 (1937); **6**, 1–17 (1941).

[5] We want to thank Professor P. Bernays for suggesting to us the present form of the set *Tr* which is more convenient than the definition of *Tr* we used before. It may be noted in passing that if instead of the class *Tr* we take the proposition function $(g)(EX)(g;m \epsilon X \text{ and } R(m, X))$ as $Tr(m)$, we can also prove the following theorem: In the system obtained from L' by omitting all the classes X not definable without using bound large variables, we can prove, for each given proposition P_m of L and $L\phi$, a theorem stating that $Tr(m)$ if and only if P_m. In other words, if we want, instead of a true set, merely a truth definition for L and $L\phi$, it suffices to use a system weaker than L'.

[6] The argument of this paragraph was communicated to us by Dr. John G. Kemeny in conversation.

[7] The following two theorems are due essentially to Professor J. Barkley Rosser who makes these points clear to us in criticizing our earlier attempts to prove the inconsistency of L' by the methods sketched in this note.

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CONTENTS

Page

ANDERSON.—The Effect of Spontaneous Assimilation on Size and Differentiation. By Constance Warwick 415

BARTHOLOMEW.—The Physiological Action of a Bacillogen Toxin on Plant Cells. By Arvin C. Brace 431

BRADLEY.—The Growth-Promoting Properties of Ground Agar. By Meloch Gerlaugh, Francis A. Hubbell and Harriet R. Mitchell 441

BRADLEY.—Further Studies on the Fixing and Preserving Mixtures of Tarr-Apathy. By C. W. Kidder, Thomas C. Bradley, R. E. Parks, Jr., and M. R. Hoagland 455

CARPENTER.—Physical Chemical Basis of Buffer Action in Biological Phenomena. By S. Bachrach 469

CHAMBERS.—Compressed Tissues and Annular Grooves and Ridges. By Edward Ellenberg and Samuel McLean 485

MARTIN.—Equations of the Conservation of Axons Systems. By Hao Wang 501